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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/084,139	02/28/2002	Shigekazu Nagata	1110-0307P	7006

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EXAMINER

O HARA, EILEEN B

ART UNIT	PAPER NUMBER
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1646

DATE MAILED: 02/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/084,139	NAGATA ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Eileen B. O'Hara	1646	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 07 November 2005.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-8, 10-14 and 18 is/are pending in the application.
- 4a) Of the above claim(s) 1-7 and 10-14 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 8 and 18 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 1-7 and 10-14 are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 28 February 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)             | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                                    |

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### **DETAILED ACTION**

1. Claims 1-8, 10-14 and 18 are pending in the instant application. Claims 8 and 18 have been amended as requested by Applicant in the Paper filed November 7, 2005.

Claims 1-7 and 10-14 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 8 and 18 are currently under examination.

### ***Withdrawn Objections and Rejections***

2. Any objection or rejection of record which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

### ***Maintained Rejections***

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

#### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3.1 Claims 8 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Barr et al., U.S. Patent No. 5,652,210, effective priority date Nov. 15, 1993, and further in view of Palmer et al., U.S. Patent No. 5,776,718, priority date March 24, 1995, or Du et al., BBRC, Vol. 226, pages 595-600, Sept. 24, 1996, or Braun et al., J. Exp Med., Vol. 183, pages 657-661, February 1996, or Baker et al., Journal of Experimental Medicine, Vol. 183, June 1996, pages 2645-2656, for reasons of record in the previous office action mailed July 6, 2005 at pages 11-13.

Applicants traverse the rejection and state that they believe that the amendments to the claims sufficiently define the invention such that it is not suggested by or obvious over the reference teachings. Applicants' arguments have been fully considered but are not deemed persuasive, because the claimed method of treatment remain obvious over the reference teachings.

3.2 Claim 8 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Lynch et al., Patent No. 5,620,889, effective priority date Oct. 13, 1994, and further in view of Palmer et al., U.S. Patent No. 5,776,718, priority date March 24, 1995, or Du et al., BBRC, Vol. 226, pages 595-600, Sept. 24, 1996, or Braun et al., J. Exp Med., Vol. 183, pages 657-661, February 1996,

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or Baker et al., Journal of Experimental Medicine, Vol. 183, June 1996, pages 2645-2656, for reasons of record in the previous office action mailed July 6, 2005 at pages 11-13.

Applicants traverse the rejection and state that they believe that the amendments to the claims sufficiently define the invention such that it is not suggested by or obvious over the reference teachings. Applicants' arguments have been fully considered but are not deemed persuasive, because the claimed method of treatment remain obvious over the reference teachings.

### *New Rejections*

#### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bellgrau et al., U.S. Patent No. 5,759,536, effective priority date January 26, 1995, and further in view of Lynch

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et al., Patent No. 5,620,889, effective priority date Oct. 13, 1994, and further in view of Palmer et al., U.S. Patent No. 5,776,718, priority date March 24, 1995, or Du et al., BBRC, Vol. 226, pages 595-600, Sept. 24, 1996, or Braun et al., J. Exp Med., Vol. 183, pages 657-661, February 1996, or Baker et al., Journal of Experimental Medicine, Vol. 183, June 1996, pages 2645-2656.

Claims 18 encompasses a method of treating graft versus host disease (GVHD) comprising administering a humanized anti-Fas ligand antibody.

Bellgrau et al. teach anti-Fas ligand antibodies (column 9, line 1, column 12, lines 40-45). Bellgrau et al. do not teach humanized anti-Fas ligand antibodies, or method of treating GVHD.

Lynch et al. teach humanized monoclonal antibodies to Fas, and teach that such antibodies can be used therapeutically to inhibit Fas ligand mediated apoptosis of cells (abstract, column 2, lines 18-52. Lynch et al. do not teach that a Fas-mediated disorder is GVHD.

Palmer et al. teach that ICE is involved in the signal transduction of Fas-mediated apoptosis, and that ICE inhibitors may be used in the treatment of graft versus host disease by inhibiting Fas signaling (column 30, line 57 to column 31, line 22).

Du et al. teach that a hammerhead ribozyme that targets both Fas-ligand and perforin mRNAs, can be used in a method of treating GVHD.

Braun et al. discloses experiments in a mouse GVHD model in which donor cells from Fas-L deficient mice delayed the onset of GVHD versus compared to donor cells that had functional Fas-L (Figure 4a), and teach that the development of therapeutic strategies aimed at controlling this cytolytic pathway (in addition to perforin, which was also shown to be an important mediator of GVHD) during bone marrow transplantation may be an approach for decreasing the risk of GVHD (page 660, last paragraph).

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Baker et al. performed experiments in a murine model of GVHD in which donor cells from FasL deficient mice or FasL expressing were transplanted into mice, and the effects compared. Recipients receiving cells from FasL deficient mice had greatly diminished GVHD symptoms, and the authors concluded that Fas-mediated cytotoxicity plays an important role in the pathophysiology of hepatic and cutaneous GVHD after bone marrow transplantation between MHC- matched allogeneic mice (pages 2649-2654).

It would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to use the anti-Fas ligand antibodies of Bellgrau et al., and make humanized versions of the antibodies as taught by Lynch et al., since humanized antibodies would be more immunologically tolerated by humans. It would also have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to use the antibodies in a method of treating GVHD, since Palmer, Du, Braun and Baker teach or suggest that the Fas pathway is at least partly responsible for some of the effects in GVHD. The skilled artisan would be motivated to do so because of the large number of transplants done and the need to reduce GVHD. There would be a reasonable expectation of success, since the method of making humanized antibodies was well known in the art, and such antibodies would be expected to be an effective inhibitor of the Fas pathway.

It is believed that all pertinent arguments have been answered.

### ***Conclusion***

5. No claim is allowed.

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Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (571) 272-0878. The examiner can normally be reached on Monday through Friday from 10:00 AM to 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached at (571) 272-0961.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://portal.uspto.gov/external/portal/pair>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Eileen B. O'Hara, Ph.D.

Patent Examiner



**EILEEN B. O'HARA**  
**PATENT EXAMINER**